

**Variation of ASVS Vials Consumption with respect to Duration
of Bite, Means of Transport and First-aid to Snakebite in
Bharatpur Hospital, Chitwan,
Lowland Nepal**



Research Report



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Abstract

INTRODUCTION: Snake envenoming is potentially life-threatening medical condition. Present study sought stronger factors responsible for greater consumption of anti-snake venom serum (ASVS) vials. **OBJECTIVE:** To chart the variability of ASVS vials consumption with reference to duration of bite, means of transport and adoption of first-aid. **METHODOLOGY:** The study was carried out in April to Sept. 2007 at Bharatpur Hospital which was selected because of supply of ASVS vials free of cost and concentration of victims from adjoining districts. Admitted envenomed victims/ their visitors were studied inclusively by the use of pre-tested data sheets. **RESULTS:** Total envenomed snakebite victims studied was 39 of which 36 (92%) were neurotoxin and 3 (8%) were haemotoxin. The case fatality rate was 22% (n=8). Range of ASVS vials consumed by survived victims was 4 to 94. No ASVS was applied to viper bite victims. Two victims were brought dead. The average ASVS consumed by medicated and survived neurotoxin victims was 40.6 vials. The correlation (r) of duration of bite and ASVS consumption was 0.19. ASVS consumption might not be associated with means of transportation. But, r between walking and ASVS consumption was 0.2. No victims adopted real first aid measure and hence, r between first aid and ASVS consumption could not be calculated. **DISCUSSION:** The antivenom is effective only if given early enough to neutralize the venom in the circulation prior to neurotoxicity. Present study implied that delayed arrival with neurotoxicity consumed scads of ASVS vials. Therefore, the use of large doses late in the course of envenoming was useless. Walking and body shaking means of transport resulted dissemination of venom throughout body leading to risk of death. In present study, no victims followed pressure immobilization technique. Hence, association of first aid with ASVS vials consumption could not be documented. **CONCLUSION:** Administration of ASVS vials as early as possible has immense value to snakebite management Use of large doses late in the course of envenoming was unlikely to be effective. Walking and body shaking means of transport elevate the risk of death. No victims followed the real first-aid and that might be one of the important factors of greater mortality and great use of ASVS vials in this region. It was impossible to estimate how many ASVS vials were required to cure each envenomed victim as the amount of venom injected could not be predicted and measured prior to ASVS administration.

Key words: Snakebite, Antivenom, Anti-snake Venom Serum (ASVS), First-aid, neurotoxicity, envenomation.

Introduction

Snake envenoming is uncommon but potentially life-threatening medical condition (**Currie 2000**). It is significant public health problem in many countries. Two regions where snake bite presents a particular problem are South East Asia and Africa (**WHO 2005a**). In Asia, the highest recorded incidence was 162 deaths per 100,000 population per year, determined in the eastern Terai of Nepal (cited from **Warrel 2005**).

From the community based study in Chitwan and Nawalparasi district, it was estimated that there were 110 snakebite victims and 12 deaths per 100,000 people per year (**Pandey 2007**). An average of **32** polyvalent anti-snake venom serum (ASVS) vials (10 ml each) prepared by Haffkine Pharmaceutical Company, Bombay, India was consumed for the treatment of each envenomed victims in Bharatpur Hospital, Chitwan and Kali Gandaki Hospital, Nawalparasi. The range of ASVS vials used was 6 to 89 (**Pandey 2006**). An average of **17.6** ASVS vials were consumed by each envenomed victims. Also, 72.4% of victims consumed less than 20 vials, 21.9% consumed 20 to 50 vials and 5.7% consumed more than 50 vials (**Ministry of Health, EDCD 2005**).

Although ASVS has been used for many years, there is no universal consensus in many countries on the optimal dose and protocol of its administration. Theoretically, it would appear that patients with more severe envenoming need higher doses of ASVS for effective neutralisation of circulating snake venom. The antivenom is effective only if given early enough to neutralize the venom in the circulation, prior to the neurotoxins reaching their target site, and thus prevent further development of neurotoxicity (cited from **Agrawal et al. 2005**).

Pressure immobilisation is the recommended first aid treatment for all snake bites (**Sutherland et al. 1979**). Pressure immobilisation bandaging is safe and appears to be effective first aid if applied correctly soon after the bite. A broad (15 cm) bandage is applied at the same pressure as for a sprained ankle over the entire limb. The patient must then remain completely immobilised, not just the bitten

limb. For bites on areas other than limbs the patient should be immobilised to slow the spread of venom (**Isbister 2006**).

Rationale / Justification of the study: The retrospective study of hospital record files revealed the greater number of ASVS vials consumption per envenomed victims (**Pandey 2006**). However, previous study could not assess the causative factors responsible for great administration of ASVS vials that has been of great expense for the Nepalese national economy. Hence, present study has sought factors responsible for application of greater number of ASVS vials.

The proportions of snake bite cases and deaths were higher when there was greater time taken to arrive treatment center (**Pandey 2007**) which was observed by **Sharma et al. 2004** too. However, the variation of ASVS vials consumed by each envenomed victims in relation to duration of snakebite and hospital arrival could not be noted/ available in literatures. Hence, the study would have greater endeavor to find out new approach to dwindle the use of ASVS vials.

The envenomed victims should arrive at hospital comfortably with immobilization of bitten part and body as a whole as far as possible in order to avoid systemic absorption of venom (**Warrel 2005b**). So, means of transport may also have great role to scads use of ASVS vials. Hence, this study would have significance to assure association of mode of transport to hospital and ASVS consumption.

First aid in snakebite is meant to delay absorption of venom from local site of bite to circulation during which time a victim can be carried to hospital where antivenom can be administered. From the experiments conducted by **Sutherland and others (1981)** on two monkeys with 300 micrograms of *Naja naja* venom, crepe bandage with pressure immobilization and administration of specific antivenom, it was inferred that monkey with above first aid had delayed neurotoxic features beyond 65 minutes and got recovered faster when treated with specific antivenom (cited from **Jena and Sarangi 1993**). The present study would have great significance as it would find the numeral variation of ASVS vials consumed with respect to proper first-aid adopted. In essence, it has paved the way to

management of snake-bite by the application of less number of ASVS vials. So, this study would have great significance and essential.

Objectives

General

To chart the variability of ASVS vials consumption rate with special reference to duration of bite, means of transport and adoption of first-aid.

Specific

- To know numeral variation of consumption of ASVS vials with respect to duration of snake-bite and hospital arrival.
- To find out numeral variation ASVS vials consumption with respect to means of transport to hospital.
- To calculate the percentage of snake-bite victims who adopted recommended first-aid and to see the variability of consumption of ASVS vials.

Methodology

Descriptive and quantitative study of variables: envenomed victims, duration of bite, means of transport, first-aid and ASVS vials consumed by envenomed victims was carried out between April to Sept. 2007 in Bharatpur Hospital that lies in Central and Southern Lowland Nepal. It was selected because it provides ASVS vials free of cost on the behalf of Nepal Government. So, majority of victims from Chitwan, Nawalprasi, Gorkha districts rush to this hospital.

Targeted study group was envenomed victims admitted in Bharatpur Hospital. The victims used to be treated with ASVS vials only after the development of ptosis noticeably. Entire envenomed cases were studied inclusively by the use of pre-tested data collection sheets to tap the information from envenomed victims or his/her visitors to meet up the objectives.



Photo 1: Examining fang marks of victim under observation

The study received the approval from the Nepal Health Research Council Ethical Clearance Board.

Before starting the observation and interview, the participants were requested to read/ understand the consent letter. The consent letter was in Nepali language so they understood it easily. They were not obliged to participate in our research against their interest. The right corner at the end of letter contained space for signature of victims or their relatives/visitors



Photo 2: Spouse of victim reading consent letter to sign

Those victims who were missed to meet and tap the proper information were visited at their residences.



Photo 3: Principal investigator interviewed the envenomed and medicated victims at their residents



Photo 4: Principal investigator interviewed the mother of dead victims at her resident. Her daughter died at hospital during medication

No consideration was given to whether the ASVS

application caused anaphylactic, pyrogenic or late serum reactions because the focus was on variability and correlation of ASVS vials consumption with respect to different parameters.

Data management in tabular, illustrative form was carried out by the application of Microsoft Excel.

Data analysis was done based on percentage, simple arithmetic mean and Karl Pearson's Coefficient of Correlation (r).

Results

The total of 39 envenomed snakebite victims studied in Bharatpur Hospital (Mahendra Adarsha Chikitsalaya) in Central and Southern Nepal for April to Sept. 2007. Of the total, 24 (61.5%) from Nawalparasi, 14 (36%) from Chitwan and 1 (2.5%) from Gorkha district; 21 (54%) were male, 36 (92%) were **neurotoxin** (Kraits and Cobra bites) and 3 (8%) were **haemotoxin** (Viper bites) victims.



Photo 5: Victim with Green Pit Viper



Photo 6: Swollen viper bitten hand



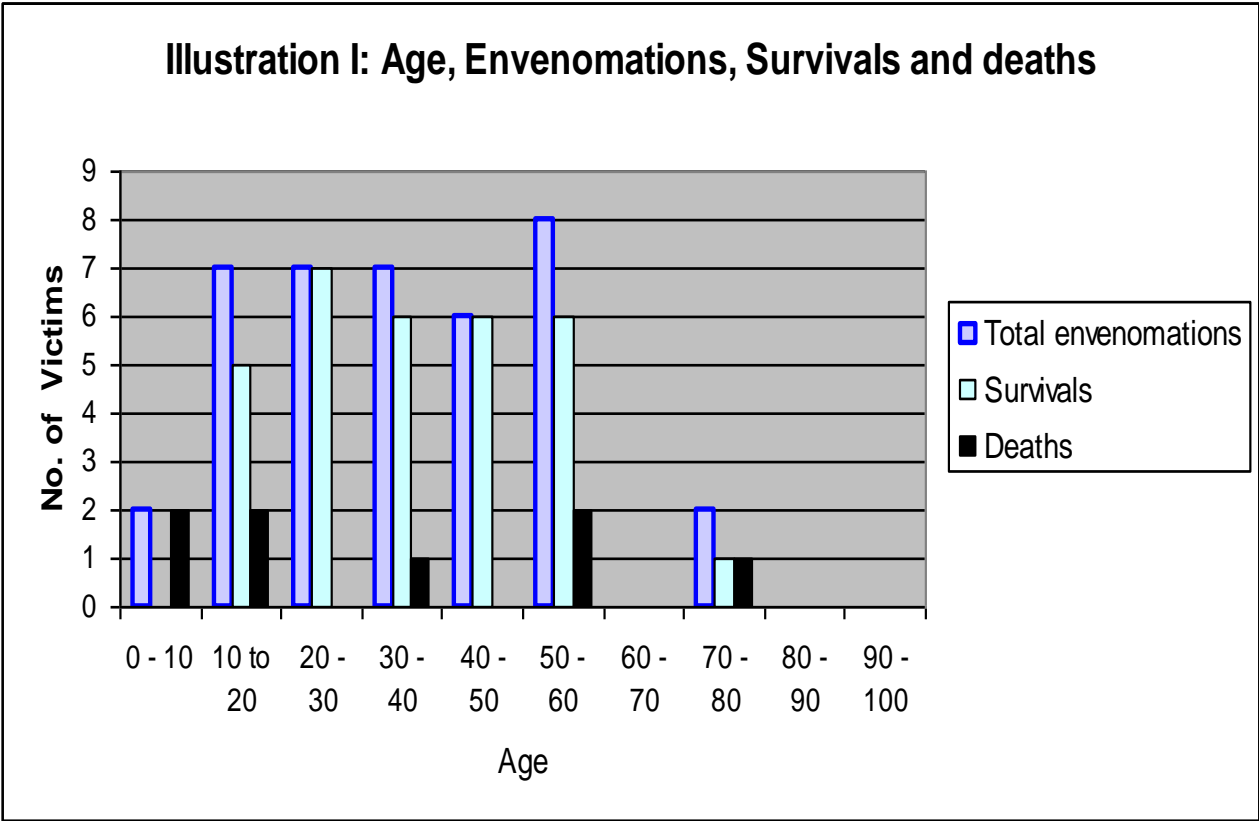
Photo 3: Viper bite victim (first from left) following traditional healing, ringing her hand on Potash solution and staying with other victims of snake bite

Viper bites were found not fatal in these regions. However, viper bites led to swelling and severe local pain. In contrary, Krait and Cobra bites were found fatal. When alleged to only neurotoxin victims, the fatality rate was 22% (n=8).



Photo 4: Body of victim

It was found that lower age was at great risk to death probably due to injection of large amount of venom per kg. body weight and poor immune system of body. Similarly, very late age might also be at risk of deaths to snake envenomations probably due to dwindling immunity (Illustration I).



Viper bite victims (n=3) were not medicated with ASVS vials. Only those who developed ptosis (n=34) were medicated with ASVS (two were brought dead). The **range of ASVS** vials consumption was 4 to 98 (10 ml each). But, when only medicated and survived victims (n=28) were considered, the range was 4 to 94. The **average ASVS** consumed by medicated and survived neurotoxin victims was 40.6 vials that were administered in average hospital stay of 3.7 days.



Photo 5: Medicating victim with Ptosis



Photo 10: Ventilating with Bladder pump

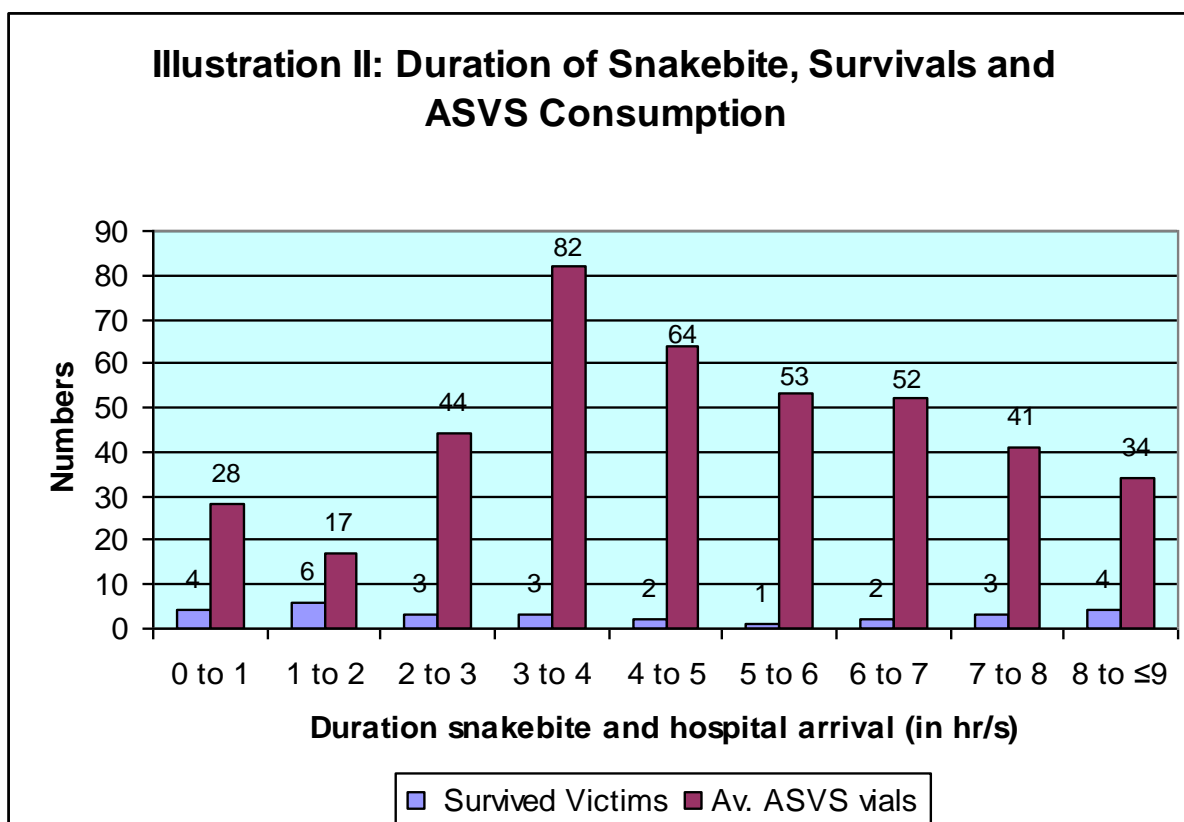


Photo 6: Ventilating with Bladder pump

{It was unfortunate that both (Photo 10 and 11) could not survive; first consumed 98 and next 70 vials of ASVS vials; both the victims arrived late at hospital with ptosis and severe neurotoxicity, their visitors brought killed Common Krait at hospital}

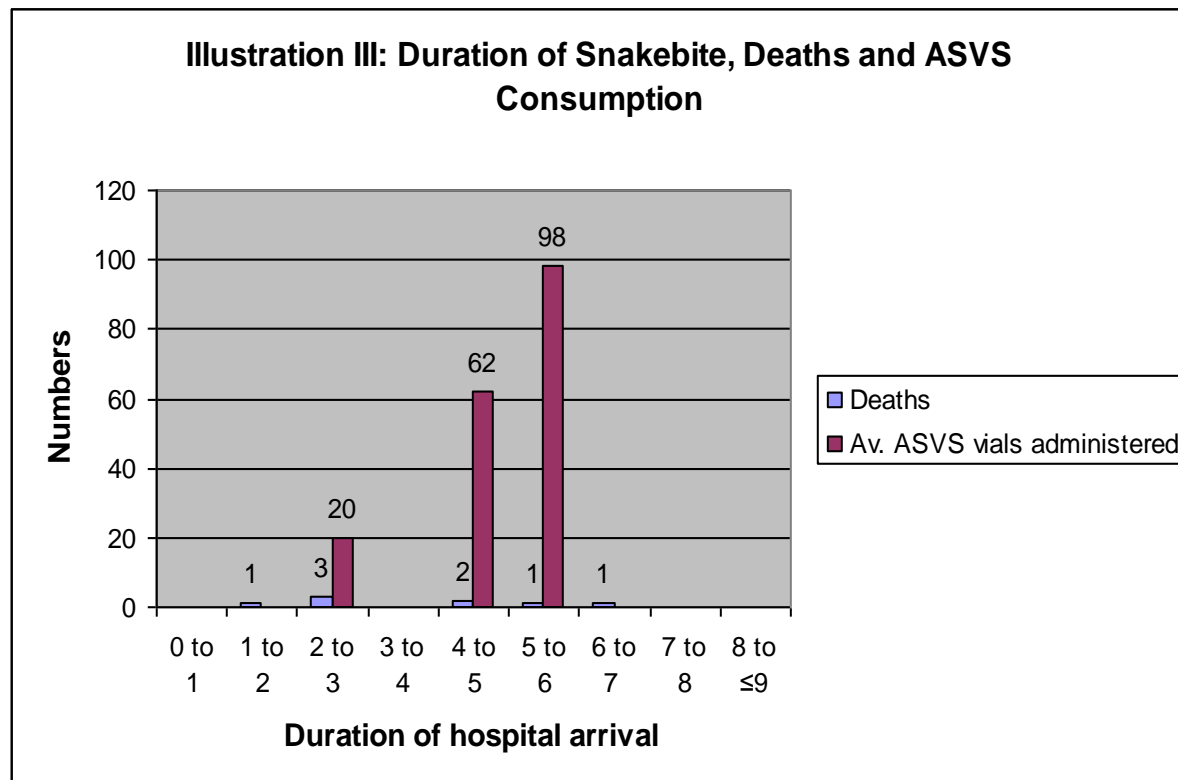
The ASVS was manufactured by Vins Bioproducts Ltd., Andra Pradesh, India (Survey No. 291). The freeze dried polyspecific enzyme refined equine immunoglobulins (ASVS) had power of specifically neutralizing venom (at dried condition) of the following species of snakes: 0.60 mg of *Naja naja* (Indian Cobra) venom, 0.45 mg of *Bungarus caeruleus* (Common Krait) venom, 0.60 mg of *Vipera russelli* (Russell's Viper) venom, 0.45 mg of *Echis carinatus* (Saw-scaled Viper) venom. ASVS was obtained from the serum of healthy equines immunized against venoms of above species of snakes (cited from leaflet in ASVS vials available in hospital). Saw-scaled Viper is not recorded in Nepal.

SN	Duration (hr)	Survived Victims	Av. ASVS vials administered
1	0 to 1	4	111/4= 28
2	1 to 2	6	102/6= 17
3	2 to 3	3	133/3= 44
4	3 to 4	3	246/3= 82
5	4 to 5	2	128/2= 64
6	5 to 6	1	53/1= 53
7	6 to 7	2	104/2= 52
8	7 to 8	3	123/3= 41
9	8 to ≤9	4	137/4= 34
	Total	28	Total ASVS vials consumed by survived victims= 1137

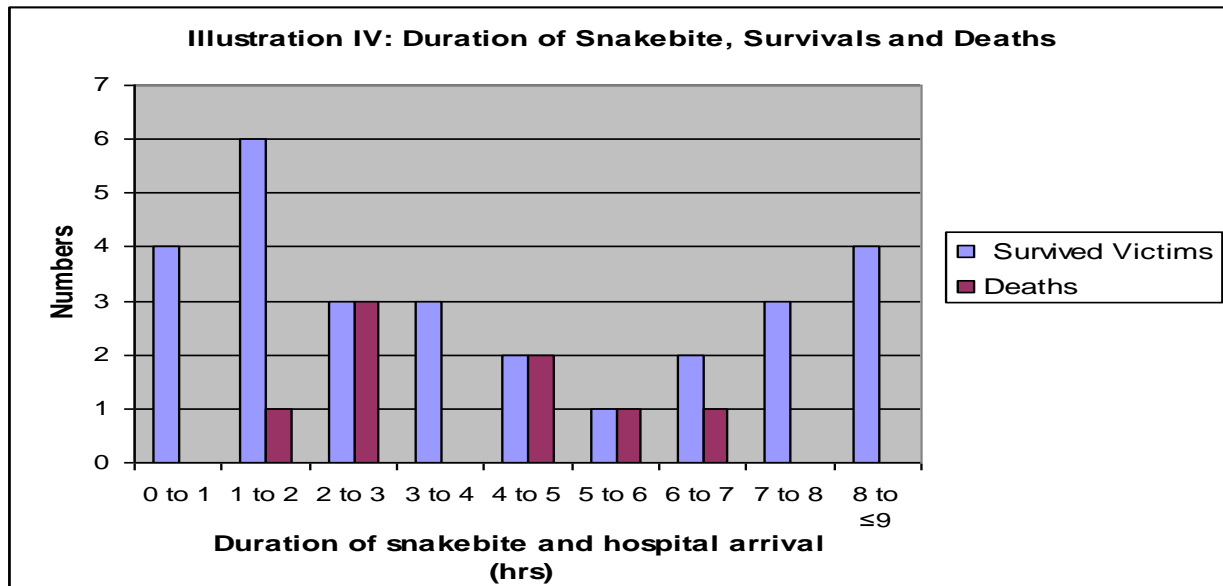


Those who arrived at hospital late (>2 hrs duration) consumed significantly greater number of ASVS vials. The correlation between duration of bite (time to hospital) and ASVS consumption (r) was 0.19.

Table 2: Duration of Snakebite, Deaths and ASVS Consumption			
SN	Duration (hr)	Deaths	Av. ASVS vials administered
1	0 to 1	–	–
2	1 to 2	1	brought dead
3	2 to 3	3	60/3= 20
4	3 to 4	–	–
5	4 to 5	2	124/2= 62
6	5 to 6	1	98/1= 98
7	6 to 7	1	brought dead
8	7 to 8	–	–
9	8 to ≤9	–	–
	Total	8	Total ASVS vials administered= 282



Furthermore, those who developed severe neurotoxicity prior to hospital arrival consumed a range of 60 to 98 ASVS vials. Moreover, delayed admittance to hospital was found risk to death/ life threatening (Illustration III , Illustration IV).



Of the 20 neurotoxin victims (Group I) who used body shaking means of transportation (cycle, cart, bike, and their use prior to van and ambulance, 5 victims (25%) died. Of the 14 neurotoxin victims (Group II) who arrived at hospital in heavy reserved vehicles (ambulance, truck) 3 victims (21%) died. Of the left over 2 neurotoxin victims (Group III) who arrived in public bus and van remained alive on treatment (Table- 3). From the study it was clear that body shaking means of transportation may be life threatening. However, it was clear that ASVS consumption might not be associated with means of transportation (Illustration V).

Illustration V: Means of Transportation, Neurotoxic Envenomations, Deaths, Av. ASVS vials Consumed by Survivals

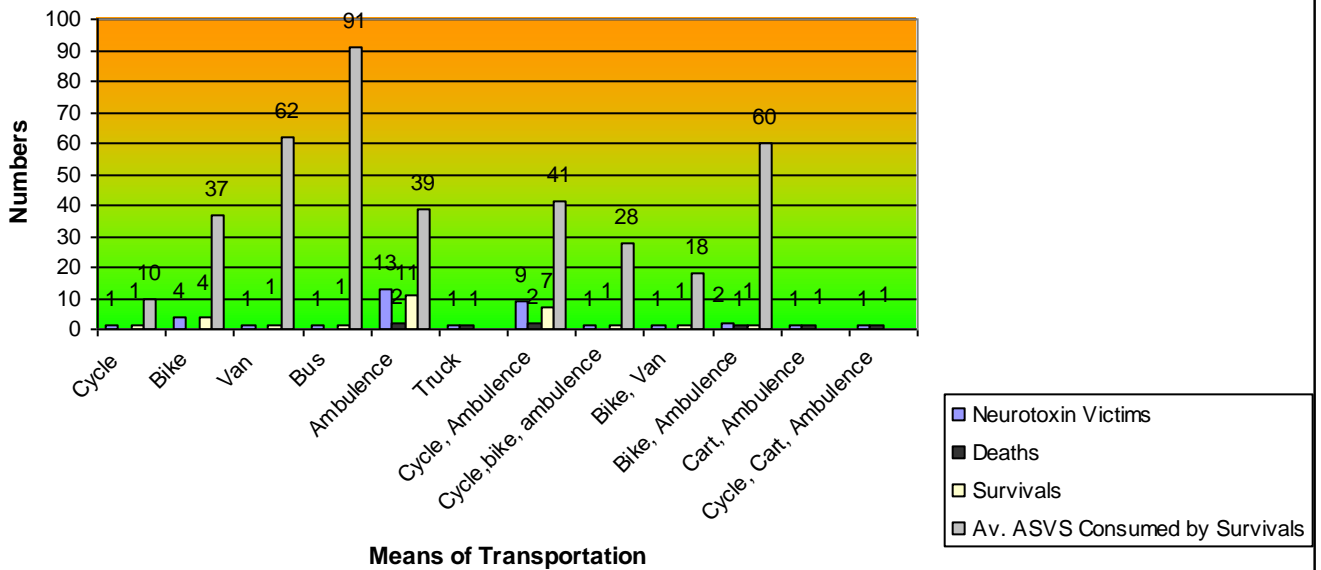
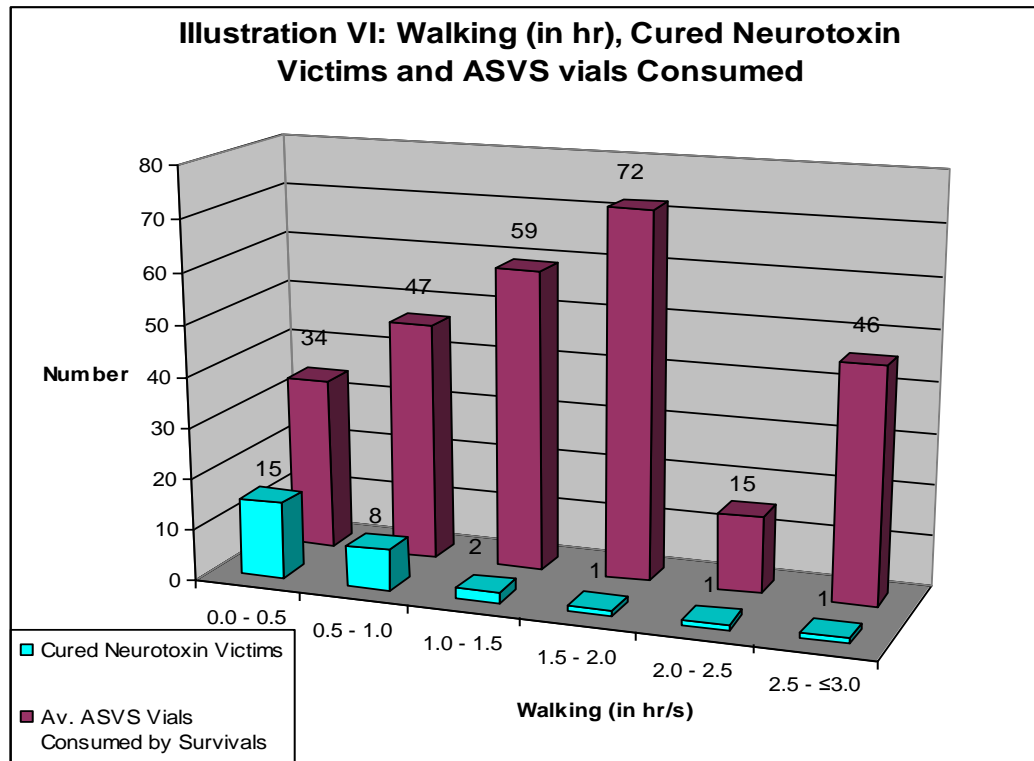


Table 3: Means of Transport, Envenomations, Deaths, ASVS vials Consumed by Survivals

SN	Means of Transportation	Envenomations	Deaths	Survivals	Av. ASVS Consumed by Survivals	Av. ASV consumed by Deaths	Remarks
1	Cycle	1	0	1	10		
2	Bike	4	0	4	37		
3	Van	1	0	1	62		
4	Bus	2	0	2	91		1 Viper Bite
5	Ambulance	14	2	12	39	124/2= 62	1 Viper Bite
6	Truck	1	1	0	0	4	
7	Cycle, Ambulance	9	2	7	41	56/2= 28	
8	Cycle, bike, Ambulance	1	0	1	28		
9	Cycle, van	1	0	1	0		1 Viper Bite
10	Bike, Van	1	0	1	18		
11	Bike, Ambulance	2	1	1	60	Brought dead	
12	Cart, Ambulance	1	1	0	0	98	
13	Cycle, Cart, Ambulance	1	1	0	0	Brought dead	
		39	8	31	Total consumed= 1137	Total consumed=282	

Moreover, who followed walking before arrival at hospital consumed significantly greater number of ASVS vials (Illustration VI). Also, the value of correlation (r) between walking and ASVS consumption was found to be 0.2. Hence, walking would be next determinant of greater consumption of ASVS vials.



A total of 69% victims adopted different types of first-aid measures! (Table 4) and left over 31% rushed to hospital without first aid attempt. Of the totality, 54% alone applied single tourniquet that was popular among rural people. It was noticed that the existing first aid practices by victims had no association with greater use of ASVS vials. Next, no victims were with first aid measures recommended by WHO. Hence, association of greater administration of ASVS vials and First aid could not be calculated.

SN	Type of First aid adopted	Envenomations	Deaths	Cured Victims	Av. ASVS Consumed by Survivals	ASVS Consumed by Deaths	Remarks
1	Single Tourniquet	21	4	15	$507/15= 34$	48+70+98	2 viper victim, 1 brought dead
2	Multiple Tourniquet	1	0	1	91	-	-
3	Crepe Bandage with Pressure Immobilization	0	0	0	0	-	-
4	Local Compression Pad	1	0	1	60	-	-
5	Tight Tourniquet	4	1	2	$81/2= 41$	8	1 viper victim
6	No first aid practice	12	3	9	$398/9= 44$	54+4	1 brought dead
Total		39	8	28	Total ASVS =1137	Total ASVS=282	

Of the totality, 16 (41%) practiced traditional treatment before hospital arrival. Of the total, 3 deaths (38%) followed traditional treatment (Table 5).

S.N.	Particulars	No. of Victims	Deaths
1	Consultation with Dhama / Jhakri (Local healers)	7	2
2	Application of Jagmohar (Garud Dhunga) i.e. Snake Stone	2	0
3	Mouth Suction	0	0
4	Herbal Medicine	0	0
5	Incision of wound	1	0
6	Ringing/deeping in Potash Solution	0	0
7	Testing Poisoning by eating chillies	2	0
8	Application of Paste by eroding sickle with stone	1	0
9	1 and Use of Kerosine in wound	1	1
10	Drinking alcohol	1	0
11	1,5, and 6	1	0
	Total	16	3

Snakes brought at hospital:

A total of four victims brought killed snakes (3 were Common Krait; 1 was Green Pit Viper) at hospital.



Photo 8: Common Krait



Photo 7: Green Pit Viper

Discussion

In present study, the **average ASVS** consumed by medicated and survived neurotoxin victims was 40.6 vials. In contrary, **Agrawal *et al.* 2005** noted an average use of 60 vials to each victim in India and **Pandey 2006** recorded an average administration of 32 vials to each victim in two hospitals of Chitwan and Nawalparasi districts, Nepal.

The antivenom is effective only if given early enough to neutralize the venom in the circulation, prior to the neurotoxins reaching their target site, and thus prevent further development of neurotoxicity (**Agrawal *et al.* 2005**). Present study also implied that delay arrival especially with neurotoxicity consumed greater number of ASVS vials. Two victims who arrived late with severe neurotoxicity (Photo 10 and 11) could not survive even though they were treated with 98 and 70 ASVS vials respectively. Therefore, the use of large doses late in the course of envenoming was unlikely to be effective. Also, The correlation between duration of bite (time to hospital) and ASVS consumption { $r = 0.19$ } also clearly depicted the value of early arrival at hospital with facility of administration of ASVS vials enough.

Means of transportation were found no associated with the greater consumption of ASVS vials (Illustration V). However, from the study it was clear that body shaking means of transportation may be

life threatening (Table 3) because of quick dissemination of venom to target tissue. Moreover, who followed walking before arrival at hospital consumed significantly greater number of ASVS vials. However, the value of correlation (r) between walking and ASVS consumption was found to be 0.2. Hence, walking would be next determinant of greater consumption of ASVS vials. But, greater use of ASVS vials might rely on amount of venom injected by snake and also on its dissemination directly via blood stream or via lymphatic channels.

Pressure immobilization bandaging is safe and appears to be effective first aid if applied correctly soon after the snakebite (**Isbister 2006, Sutherland *et al.* 1979**). In present study, no victims followed pressure immobilization technique. Hence, correlation between world widely followed first-aid technique and consumption of ASVS vials could not be assessed.

The amount of venom injected at a bite seems to be very variable (**Myint *et al.* 1985, Phillips *et al.* 1988**). Very large doses of antivenom may be required to treat patients bitten by species capable of injecting enormous amounts of venom or extremely potent venom. A victim bitten by the King Cobra (*Ophiophagus hannah*) was given 1150 ml (115 vials) of specific antivenom and prolonged artificial ventilation (Tin *et al.* 1991). Hence, beside above factors, the amount of venom injected/circulated in victims' body might have significant correlation with great consumption of ASVS vials.

The ASVS administered at present study was polyspecific that can be just as effective as monospecific ones, but since they contain antibodies against several different venom, a large dose of antivenom must be administered to neutralize a particular venom (Warrell 2005b). Therefore, next stronger factor responsible for scads use of ASVS vials might also be the use of polyspecific ASVS.

Most rural snakebite victims (56%) consulted or depended on traditional healers (**Pandey 2007**). In contrary, 41% of the total victims consulted traditional healers/ attempted traditional healing methods in present study. But Snow reported that up to 80% of snakebite victims first consult traditional practitioners before visiting a medical center in rural Kenyan Population (**Snow 1994**). Over all data depicted that awareness to snakebite management is gradually alleviating in Nepal. Present study noted 54% victims

who followed single tourniquet. Majority of tourniquet applied in rural areas were ineffective in preventing the systemic spread of venom (Warrell 1992, Warrell 1990). Lymphatics are the main route of venom than a vein (Jena and Sarangi 1993). Hence, pressure immobilization technique of first aid would be best in this region.

Present study revealed a total 61.5% from Nawalparasi and 36% from Chitwan where as **Pandey 2007** recorded 63% from Nawalparasi district and 37% from Chitwan. From the facts, it was evident that snakebite health hazard is more epidemic in Nawalparasi than in Chitwan. Present study recorded 54% male victims that were also noted by **Devekota et al. 2000** and **Pandey 2007**. Similarly, **Devekota et al. 2001** recorded 53% male; **Bista et al. 2005** accounted 51.3% male snakebite victim and **Pandey 2006** noted 49% male victims.

Conclusion

Administration of ASVS vials as early as possible has immense value to snakebite management with less no. of ASVS vials that are expensive and occasionally scarce in Nepal. Use of large doses late in the course of envenoming was unlikely to be effective.

Walking and body shaking means of transport should be avoided as far as possible to minimize the risk to death and also to greater consumption of ASVS.

Variability and greater administration of ASVS vials with respect to recommended first-aid could not be assessed because of null victims with real first-aid. The popular tourniquet in this region was found ineffective.

The amount of venom injected could not be predicted and measured prior to ASVS administration. Therefore, it was impossible to estimate how much ASVS vials were required to cure each envenomed victims.

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Recommendation

1. Concerned authorities should launch awareness training programs on first aid to snakebite throughout the rural Nepal especially to farmers.
2. People should be made aware to 'need of delivery of snakebite victims as quickly as possible without shaking the body of the victims'.
3. Similar researches should be conducted in wide range to find out the factual results.
4. Application of monospecific ASVS should be arranged from Nepal government.
5. Toxinologists should be produced in Nepal to serve in Toxinology in Nepal.